Review of spinal radiosurgery: a minimally invasive approach for the treatment of spinal and paraspinal metastases

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Intracranial radiosurgery has been proved effective for the treatment of brain metastasis. The treatment of paraspinal and spinal metastasis with spinal radiosurgery represents a natural extension of the principles of intracranial radiosurgery. However, spinal radiosurgery is a far more complicated process than intracranial radiosurgery. Larger treatment volumes, numerous organs at risk, and the inability to utilize rigid, frame-based immobilization all contribute to the substantially more complex process of spinal radiosurgery.

Beyond the convenience of a shorter duration of treatment for the patient, spinal radiosurgery affords a greater biological equivalent dose to a metastatic lesion than conventional radiotherapy fractionation schemes. This appears to translate into a high rate of tumor control and fast pain relief for patients. The minimally invasive nature of this approach is consistent with trends in open spinal surgery and helps to maintain or improve a patient’s quality of life. Spinal radiosurgery has expanded the neurosurgical treatment armamentarium for patients with spinal and paraspinal metastasis. (DOI: 10.3171/FOC/2008/25/8/E18)

KEY WORDS • helical tomotherapy • metastasis • spinal radiosurgery

PARASPINAL and spinal metastases are reasonably common sequelae of cancer. The incidence of spinal and paraspinal metastasis is increasing in large part because patients with systemic cancer are living longer with chemotherapeutic improvement and, thus, run a longer risk of the complications of dissemination of their disease. Initial presenting symptoms may include pain secondary to osseous invasion of the tumor and weakness, numbness, and autonomic dysfunction secondary to spinal cord and nerve compression. If cancer has not been previously diagnosed or if the diagnosis of the paraspinal/spinal lesion is in doubt, a percutaneous neuroimaging guided biopsy can be performed to confirm the underlying pathology. Corticosteroids, pain management, radiation therapy, and surgical resection with possible fusion have been the mainstays of treatment for these patients. The selection of a treatment algorithm for these patients is complicated by the extent of their extraspinal disease (for example, metastasis to the brain, abdomen, or chest).

The management of patients with spinal and paraspinal tumors has undergone a great deal of change in the past 5 years. Significant improvements in neuroimaging, computer planning, and linear accelerator-based radiation therapy have led to the development of extracranial radiosurgery. The foundation of this emerging field rests upon the pioneering work of Lars Leksell and the more than 30 years of success with the Gamma Knife (Elekta AB). Leksell demonstrated that ionizing beams of radiation could be employed with scalpel-like precision when utilized by neurosurgeons and directed by image guidance.

The concept of radiosurgery, a high dose of radiation targeted to a pathological entity and delivered in 1–5-fractions, has proven so successful at treating both benign and malignant lesions that it changed the paradigm for radiation therapy. Radiosurgery and hypofractionated radiation therapy for benign and malignant intracranial lesions have proven very effective. The radiobiology of radiosurgery has been shown to be very favorable for tumor control. Radiosurgery has been proven to be a cost effective option compared to open surgical resection. The use of 1–5-fraction image-guided radiation therapy is typically preferred to standard 10–30-fraction schemes and is more easily tolerated by patients because it requires fewer trips to the hospital.

For patients with spinal tumors, conventional radiation therapy has been the mainstay of treatment. Radiation therapy has been utilized to arrest the tumor, control pain, and stabilize or improve neurological function. Open surgery is usually reserved for correction of spinal instability or subluxation, for patients with intractable pain, and for patients with acute or progressive neurological deficits refractory to other therapies. Spinal radiosurgery and image-guided spinal radiation therapy are now technologically achievable. Instruments such as the TomoTherapy Hi-Art treatment system (TomoTherapy, Inc.), CyberKnife (Accuray, Inc.), Novalis (BrainLab, Inc.), and Axesse (Elekta AB) have been utilized to deliver spinal radiosurgery. In this article, the current clinical indications and outcomes for such spinal radiosurgery will be examined.

Abbreviations used in this paper: BED = biological equivalent dose; EBRT = external beam radiation therapy.
The use of 3D conformal planning in the treatment of spinal metastasis has consisted of spinal and nerve root decompression with fusion for any instability and radiation therapy (following surgery). The use of 3D conformal planning in the treatment of spinal lesions is not new. Real-time image guidance and adaptive planning are, however, new concepts in spinal radiosurgery and radiation therapy. Standard treatment for metastases has been 3000 cGy in 10 fractions delivered over 2 weeks. Intraparenchymal lesions such as ependymomas and gliomas, however, are typically treated with 5000–5040 cGy delivered in 180-cGy fractions over 5 weeks. Results completed thus far in the Radiation Therapy Oncology Group Protocol No. 74-02 (RTOG 74-02) trial, the study of the Bone Pain Trial Working Party in the United Kingdom, and the Dutch Bone Metastasis study in the Netherlands have demonstrated no consequential difference between single fraction radiotherapy and multifraction schemes.

In 1995, Hamilton and colleagues first described the use of linear-accelerator-based spinal stereotactic radiosurgery. Since then, large fraction conformal radiation delivery to spinal lesions has been pursued at multiple centers using a variety of devices. Most radiosurgical centers currently utilize doses of 12–24 Gy to the margin of the treatment volume and deliver spinal radiosurgery in 1–5 fractions. The prescription dose depends in part upon the tumor location, histological characteristics, and volume as well as the fractionation scheme, surrounding organs at risk, and prior radiation therapy. Numerous studies have demonstrated the safety and effectiveness of intracranial stereotactic radiosurgery for treating metastatic disease to the brain. Local tumor control rates following radiosurgery range from approximately 85 to 95%. The superior BED achieved with stereotactic radiosurgery may explain the generally positive responses achieved for even traditionally radiation-insensitive metastases such as melanoma and renal cell carcinoma.

For metastatic lesions of the spine, broad indications for spinal radiosurgery versus traditional open surgery and EBRT are detailed in Table 1. In general, cases of spinal and paraspinal metastasis are well suited for a radiosurgical approach when they exhibit several of the following features: 1) good performance status and expected survival of > 3 months; 2) limited spinal involvement (typically 2 contiguous levels); 3) certainty of diagnosis; 4) no evidence of biomechanical instability to the spine; and 5) minimal cord compression and no appreciable neurological deficits that would warrant a decompression of neural elements. Spinal radiosurgery typically affords a favorable benefit-to-risk ratio for a patient population not well suited to either conventional EBRT or open surgery. Tumor volumes treated by spinal radiosurgery may be an order of magnitude higher than those safely treated with intracranial radiosurgery.

A number of frameless stereotactic radiosurgery devices (for example, TomoTherapy Hi-Art, CyberKnife, Axesse, Trilogy [Varian, Inc.], and Novalis) are currently available for spinal radiosurgery. Each has its own set of inherent advantages and disadvantages. Regardless of the device employed, the approach for spinal radiosurgery requires a multidisciplinary team not unlike that which would be required for an open spinal procedure. In spinal radiosurgery, the neurosurgeon is joined by a team comprised of a radiation oncologist, a neuroradiologist, a medical physicist, and a radiation technician.

Conceptually, the treatment steps for spinal radiosurgery are as follows: 1) definition of the anatomical target and radiation-sensitive adjacent structures, 2) design of a conformal radiosurgery plan, 3) determination of the dose and fractionation scheme required for effective clinical (pain and neurological function) and oncological (tumor control) outcomes, 4) verification of the treatment, 5) delivery of the treatment, and 6) immobilization and intraoperative tracking of the patient during treatment.

Utilizing CyberKnife radiosurgery, Gerszten et al. treated 125 spinal lesions in 115 consecutive patients. In this series, 108 of the lesions were metastatic and 78 of the patients had undergone prior EBRT. Tumors were treated with a mean dose of 1750 cGy (range 1250–2500 cGy). In patients with benign spinal tumors, tumor control following CyberKnife radiosurgery was 100%, but no assessment of tumor control was made for those with malignant spinal tumors. In those with pain prior to treatment, 94% experienced improvement in their axial and radicular pain. No acute radiation toxicity was observed in this series.

In another case series, 16 patients with a variety of spinal lesions were treated with CyberKnife radiosurgery. After at least 6 months of follow-up, none of the patients had experienced radiation-induced complications or disease progression.

De Salles et al. reported on the treatment of 14 patients with 22 spinal lesions. Following Novalis radiosurgery,

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**TABLE 1**

| Indications for Open Surgery, Spinal Radiosurgery, and EBRT in Patients with Spinal Metastasis* |
|---------------------------------------------------------------|---------------------------------------------------------------|---------------------------------------------------------------|
| **Indications for** | **Indications for** | **Indications for** |
| **Traditional Spinal Surgery** | **Spinal Radiosurgery** | **EBRT to the Spine** |
| biomechanical instability of the spine | no biomechanical instability | extensive (≥2 levels) spinal involvement |
| significant cord compression | no appreciable cord compression | poor performance status (KPS < 70) |
| acute or progressive neurological decline | minimal or fixed neurological deficits | palliative approach (<3 mos expected survival) |
| uncertain Dx & need for histological exam | certainty of diagnosis | stable or fixed neurological deficits |
| KPS ≥ 70 and > 3 mos expected survival | metastatic disease involving ≤ 2 contiguous spinal levels | certainty of diagnosis |
| | KPS ≥ 70 & > 3 mos expected survival | |

* KPS = Karnofsky Performance Scale score.
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50% of the patients experienced improvement in their pain. Tumor control was achieved in 56% of spinal tumors. Using similar methodology, Benzil et al. \(^1\) reported pain relief in 32 of 34 patients treated, although they also reported an increased risk of radiculitis in those receiving a BED > 60 Gy. Ryu et al. \(^2\) noted improvement in pain in 85% of patients treated with spinal radiosurgery; a more recent report from that same group showed continued success with regard to pain management. \(^23\) They did, however, observe a 5% radiological progression of metastatic disease to levels adjacent to those treated.

More recently, Degen et al. \(^3\) treated 51 patients with 72 spinal tumors using CyberKnife radiosurgery. The majority (52.8%) of these patients had prior EBRT. Tumors were treated with a mean dose of 2116 cGy in an average of 3 fractions. With a mean follow-up period of 1 year, pain was improved in the vast majority of patients; this effect proved durable too. Quality-of-life outcome measures were also maintained throughout the length of the study. Complications were generally few and self-limited. In those patients who had not undergone prior irradiation, tumor control in this short study was 100%. Gerszten et al. \(^4\) demonstrated 92% improvement in pain for patients with spinal metastases undergoing CyberKnife radiosurgery and kyphoplasty.

The largest spinal radiosurgery experience to date is that of Gerszten and colleagues\(^5\) at the University of Pittsburgh. In a series of 500 patients treated for spinal metastases with CyberKnife radiosurgery, Gerszten and colleagues\(^5\) reported long-term pain improvement in 86% and local tumor control in 90% of patients. Recent publications by other groups demonstrate radiological and quality of life outcomes that are comparable to or superior to those of radiation therapy. \(^11,23\) Most employ an 8- or 10-Gy dose limitation to the adjacent spinal cord volume to limit short- and long-term radiation-induced cord toxicity.\(^11,12,23,33,39\) Jin et al. \(^23\) recommend limiting the 10% of the adjacent spinal cord volume to a dose of ≤ 10 Gy. Maximal tolerable dose and dose-volume constraints for organs at risk (for example, kidney, esophagus) near spinal tumors are even less well defined and generally must be extrapolated from the radiation therapy literature.\(^24\)

The major limiting factor for effective treatment is the tolerance of the spinal cord and other organs at risk. Traditional radiation therapy tenets hold that the spine can tolerate 4500–6000 cGy in daily fractions of 180–200 cGy with a < 5% risk of myelopathy in 5 years’ time.\(^3,10\) Early and late forms of radiation toxicity to the spine include the L’Hermitte sign, acute paralysis secondary to ischemia, lower motor neuron disease, and tissue necrosis. The issue of repeated irradiation is less well studied. Animal and clinical studies do suggest that spinal lesions can be retreated with meaningful doses leading to favorable outcomes.\(^2,23\) The effective BED between single or hypofractionated high-dose and traditional fractionated radiation therapy remains to be accurately determined.

Additional complications that have been reported with spinal radiosurgery include esophagitis, paresthesias, fatigue, dysphagia, nocturia, diarrhea, radiculitis, and laryngitis. Fortunately, these complications appear rare when modern dose planning and the aforementioned doses and fractionation schemes are employed.\(^7,16,23\) The radiosurgical dose tolerance for organs at risk, such as the esophagus, kidney, trachea, and colon, must be better delineated.

Experience at the University of Virginia

At the University of Virginia, a multidisciplinary spinal radiosurgery program was initiated in 2004. At approximately that same time, one of the first helical tomotherapy units was installed at our university.

Our TomoTherapy Hi-Art treatment system is very similar to a diagnostic CT scanner, but, in addition, it has a megavoltage radiation source and a state-of-the art multileaf collimator modulating the radiation delivered. The 64-leaf binary multileaf collimator is 40 cm long, with 6-mm leaves mounted onto a CT gantry. The collimator rotates while the patient advances on the table. The TomoTherapy system is capable of delivering conformal radiation therapy or radiosurgery to small or rather large fields. Using the on-board megavoltage CT scanner, images can be acquired and coregistered to planning images. These megavoltage CT images can be used to position the patient to within 1-mm anatomic accuracy compared to predelivery data.

Unlike Gamma Knife surgery (which is performed using the Gamma Plan dose planning software), tomotherapy utilizes an inverse planning system. Target and avoidance structures are contoured and each is assigned a dose minimum and maximum. A computer then determines the blocking positions required to deliver the optimal treatment within the aforementioned constraints. A typical helical tomotherapy dose plan and dose-volume histogram for treatment of a spinal metastasis is depicted in Fig. 1.

To date, more than 100 patients have been treated by means of helical tomotherapy through the University of Virginia’s radiosurgery program, and many of these patients have had paraspinal and spinal metastases. Tumor histological types treated thus far include traditionally radiation-sensitive metastases (for example, non–small-cell lung cancer, breast cancer, esophageal cancer, and prostate cancer) and radiation-insensitive ones (such as melanoma and renal cell carcinoma). At our center, we typically prescribe a radiosurgical dose of 18–24 Gy to treat paraspinal and spinal metastases. The mechanisms by which tumor growth is arrested and pain relief is afforded are not likely to be different from those involved in traditional radiation therapy, but the higher BED delivered by spinal radiosurgery as compared to EBRT may be responsible for the rapid pain relief patients experience after spinal radiosurgery and the ability of the technique to effectuate a positive response in radiation-resistant tumor types (for example, melanoma and renal cell carcinoma). Overall, fairly rapid pain relief (often in < 1 week), as assessed on a visual analog pain scale, has been observed in these patients.

In-field failure seems rare, but out-of-field failure in other areas of the neuraxis has been observed. To date, in patients who have undergone spinal radiosurgery for the treatment of metastatic disease, we have only observed only 1 in-field failure. This speaks to the need for close clinical and radiological follow-up for these patients; we recommend clinical and neuroimaging follow-up at 3-month intervals following treatment. No overt neurotoxicity has been noted with spinal radiosurgery at our institution even in patients who have previously received convention-
al radiation therapy to the same area. In particular, we have not observed cord toxicity related to spinal radiosurgery when we limit the dose to \(\leq 8\) Gy to the region of the spinal cord immediately adjacent to the levels involved with metastatic disease.

Certainly, the planning and delivery process is far more complex in spinal radiosurgery than in conventional radiation therapy to the spine. Fortunately, in a study using dynamic MR imaging to evaluate thoracic spinal cord motion in patients treated at the University of Virginia, minimal motion of the cord was seen when patients were placed in a traditional type of body-fixation system.\(^6\) An expansion of the treatment volume by 0.5 mm seemed prudent based upon the small motion that was detected.

**The Future**

Although the field of spinal radiosurgery remains in its infancy, the aforementioned series as well as our institutional experience clearly show a role for it in the treatment of spinal and paraspinal metastases. Radiosurgery can be utilized as a salvage treatment for those who have already undergone EBRT yet demonstrate persistent symptoms and/or radiological progression. In addition, spinal radiosurgery can be used as an initial treatment for patients with limited spinal disease, favorable overall performance status, and focal neurological symptoms. It can also be used in conjunction with other minimally invasive approaches such as kyphoplasty, vertebroplasty, and endoscopic decompressive or stabilization spinal procedures.\(^{15,17}\)

Extrapolating from the intracranial radiosurgery literature, spinal radiosurgery should also have a role in the treatment of some benign spinal lesions, although this role is not well defined and further clinical and perhaps even preclinical studies are needed.\(^4,10\)

**Conclusions**

Neurosurgical application of spinal radiosurgery remains in its infancy. Extrapolating from the successes of intracranial radiosurgery, radiosurgical principles appear to offer a favorable benefit-to-risk ratio for malignant tumors of the spine. Preliminary application of stereotactic radiosurgery for spinal and paraspinal metastasis appears promising, but the efficacy and, in turn, the indications for this approach are at present not fully defined. Further studies will shed light on the role of stereotactic radiosurgery in the neurosurgical treatment armamentarium for patients with spinal metastases.

**References**

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